REMARKS

Claim 1 is amended and claims 22-32 are new. Basis for the amendments to claim 1 is, for example, in paragraphs 11, 35 and 36 of the specification, and in originally filed claim 1 as it referenced a viral envelope protein. Claim 1 is amended to clarify the invention and the amendment is not narrowing. Representative basis for claims 22 and 23 is in paragraph 53, representative basis for claim 24 is in paragraph 84, and representative basis for claims 25 and 26 is in paragraph 85, for example. Representative basis for claims 27, 28, 29 and 31 is in paragraph 41, and representative basis for claims 30 and 32 is in paragraphs 83 and 107 and in Figure 6, for example. Accordingly, amendments to claim 1 and new claims 22-32 add no prohibitive new matter.

Applicant notes and appreciates the withdrawal of the rejection in the previous Office action. In the most recent Office action, the Office rejected claims 1, 2, 4, 5 and 9-14 for alleged obviousness under 35 U.S.C. §103(a) in view of Bieniasz and Mohler. The Office also rejected claims 1, 2, 4, 5 and 9-14 for alleged obviousness under 35 U.S.C. §103(a) in view of Moir and Mohler. The Examiner clarified the latter rejection also was directed to claim 21 in a telephonic interview with the undersigned representative on May 19, 2006.

Claimed matter is *prima facie* obvious only when a combination of cited documents (1) teaches or suggests all of the claimed elements, (2) the person of ordinary skill in the art was motivated to modify the document(s) as suggested in the Office action, and (3) there was a reasonable expectation of success. *See* MPEP 2142, *et seq*. Applicant has amended claim 1 to clarify cell fusion is mediated by a viral envelope protein. Applicant respectfully traverses the outstanding rejections in the Office action because there was no motivation to combine the cited documents and arrive at the claimed invention.

The Court of Appeals for the Federal Circuit (CAFC) in *In re Rouffet*, 47 USPQ.2d 1453 (Fed. Cir. 1998), reversed a finding of unpatentability by the Board of Appeals on the basis there was no motivation to combine the documents cited for the rejection of Rouffet's claims, as described in the previous Office action response. Applicant shows hereafter the bases for motivation to combine documents discussed in *In re Rouffet* are not present, and provides additional legal precedent underscoring the lack of motivation to combine the cited documents.

The Cited Documents Address Different Problems

The first listed basis in *In re Rouffet*, "the nature of the problem to be solved," is not found here as the studies in Mohler are limited to detecting complementary beta-galactosidase fragments in unmodified mouse cells. There is no mention of assays in which cell fusion is mediated by a viral envelope protein. Bieniasz and Moir discuss cell fusion assays using modified cells that express a viral envelope protein, and fusion is assessed by a trans-activating promoter/reporter readout, which is different than the claimed method. Because Mohler fails to mention cell fusion assays mediated by a viral envelope protein, the person of ordinary skill in the art would not have combined Mohler with Bieniasz or Moir due to differences in the problems to be solved.

On page 4 of the Office action, the Office states the "Conclusions" section of Mohler provides the motivation to combine Mohler with the other cited documents. The first sentence in this section states the *lacZ* reporter system described "can be further extended in multiple new directions." The Office, however, does not take into account the remaining sentences in this section, in which the authors define the types of systems to which the *lacZ* reporter system could be applied. The remaining sentences in this section mention suggest application of the *lacZ* reporter system to (1) co-transduction of cells, (2) determining whether proteins derived from two active genes are coincident or co-localized in a cell, (3) microscopic detection, quantitation and kinetics of myoblast fusion, (4) determination of cell lineage in transgenic animals, (5) protein-protein interactions by the study of chimeric proteins, and (6) translocation of proteins within a cell. None of these applications pertain to the same problem addressed by the claimed methods: assessing cell fusion mediated by a viral envelope protein. Thus, Mohler fails to address the problem addressed by Bieniasz and Moir and the pending claims, and therefore there was no motivation to combine it with the other cited documents.

The Cited Documents Themselves Provide No Motivation for Modification

The second basis, "the teachings of the prior art," is not found here either as there is no motivation provided by the documents themselves. The studies in Mohler are limited to (1) native NIH-3T3 cells co-transduced with complementary beta-galactosidase fragments, and (2) native C2F3 myoblast cells separately transduced with beta-galactosidase fragments, which are cells that fuse under certain conditions. The first study described in Mohler using NIH-3T3 cells is not pertinent to the method of claim 1 since cells expressing the viral envelope protein and cells

expressing the envelope protein receptor are separately transduced, not co-transduced, with complementary reporter fragments. The second study is not pertinent to the method of claim 1 because the claimed fusion processes are mediated by a viral envelope protein, and do not result from fusion of native cells.

The studies in Mohler also are inapplicable to claims 22 and 23 because the latter claims specify one of the reporter fragments consists essentially of the N-terminal alpha region of a beta-galactosidase protein. Such a fragment is not disclosed or suggested in Mohler, as far larger fragments are studied (*see* Figure 1 on page 12424 of Mohler). The studies in Mohler also are inapplicable to claims 27-32 as the specific cell types specified in these claims are not disclosed or suggested.

As discussed above, the "Conclusions" section in Mohler fails to address assays in which cell fusion is mediated by a viral envelope protein. Thus, there is no teaching or suggestion in Mohler that the *lacZ* systems described should be applied to viral envelope-mediated cell fusion assays, and therefore, there was no motivation to combine it with Bieniasz and Moir.

Bieniasz and Moir also provide no motivation to apply the *lacZ* system of Mohler with viral envelope mediated assays. Rather, Bieniasz and Moir report the assays described therein are fully functional and no modification is stated as necessary or desirable. This lack of a suggestion to modify the assays in Bieniasz and Moir is addressed in greater detail hereafter.

<u>There is No Showing the Knowledge and Ordinary Skill in the Art Provided a Motivation to Combine the Cited Documents</u>

The third basis in *In re Rouffet* is "the knowledge of persons with ordinary skill in the art." In order to apply this basis, the Court in *In re Rouffet* stated it would be necessary to "explain what specific understanding or technological principal within the knowledge of one of ordinary skill in the art would have suggested the combination" and concluded that "the Board merely invoked the high level of skill in the field of the art. If such a rote indication would suffice to supply a motivation to combine, the more sophisticated scientific discovery would rarely, if ever, experience a patentable technical advance." The CAFC further commented that the knowledge of persons of ordinary skill in the art may include certain references of special importance (i.e., that one or both of the cited documents is so well know that anyone in the art would be familiar with the documents). An example would be the famous Kholer and Millstein paper on monoclonal antibody preparations.

There is no suggestion in the documents themselves that it would be desirable to modify the readout of the assays utilized in Bieniasz or Moir. Rather, the documents report the assays described are functional and no modification is suggested. The Office's statement also does not explain the specific understandings or technological principals that would lead to combining the documents, as required. And the documents cited do not rise to the level of importance that they can be deemed documents of special importance. Thus, there is no showing the level of ordinary skill in the art was sufficient to combine the cited documents and arrive at the claimed methods.

Thus, the standards for combining documents set forth in *In re Rouffet* are not met by the cited documents.

Each Combination Does Not Suggest the Desirability of the Claimed Methods

The CAFC in *In re Fulton*, 73 USPQ.2d 1141 (Fed. Cir. 2004), emphasized a proper inquiry is "whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination (emphasis added)." The Office states that applying the *lacZ* readout system in Mohler to assays in Bieniasz and Moir would reduce false positive signals and increase the accuracy of the methods (Office action, page 4). Bieniasz and Moir, however, do not suggest there is a problem associated with false positive signals or with accuracy, and therefore, there was no suggestion to modify the fusion methods discussed in these documents.

Specifically, Bieniasz on page 2600 states the reporter construct utilized therein produced "only very low levels of SEAP activity" when there was no fusion, and "high levels of SEAP" were secreted by the transfected cells upon fusion. Bieniasz concluded the "assay accurately and specifically" measured cell fusion between cells comprising an HIV-1 envelope protein and cells comprising its receptor. Similarly, Moir concluded the assay system reported therein offered "a biologically significant model for studying fusion events with the advantages of being rapid, reproducible, and versatile" (Abstract). There also is no evidence in Mohler that the *lacZ* readout system should be applied to assays in which cell fusion is mediated by a viral envelope protein, as addressed above.

Thus, Bieniasz and Moir do not suggest modifying the readout of the reported fusion assays would have been desirable. Accordingly, a person of ordinary skill in the art would not have modified the assays described in these documents with the *lacZ* readout discussed in Mohler.

There is No Evidence that Modifying the Cited Documents Would Result in an Advantage

Recognition by a person of ordinary skill in the art that modifying elements of the cited documents would have resulted in an advantage or expected beneficial result could be a basis for finding a motivation to combine them (*In re Sernaker*, 217 USPQ 1, 5-6(Fed. Cir. 1983)). No such advantage, however, is suggested by the cited documents. As noted above, Bieniasz and Moir state the fusion assays are useful as reported, and there is no suggestion in either document that there would be an advantage to modifying assay readout. Further, Moir does not suggest the *lacZ* reporting system could be advantageously applied to fusion assays mediated by a viral envelope protein. And there is no evidence that modifying the assay readout of Bieniasz or Moir with a *lacZ* readout would have resulted in an improved fusion assay before Applicant's disclosure. Thus, each combination fails to suggest there would have been an advantage provided by the claimed methods, and therefore, there was no motivation to combine the cited documents.

* * *

In conclusion, there was no motivation to combine the cited documents because (1) the cited documents address different problems, (2) the documents themselves provide no motivation for modification, (3) the knowledge and ordinary skill in the art provided no motivation for modification, (4) there is no suggestion in each combination that modification was desirable, and (5) there is no suggestion in each combination that modification was advantageous. The claimed methods therefore are not *prima facie* obvious. Accordingly, it is respectfully requested the Office withdraw the rejections of the claims under 35 U.S.C. §103(a).

Information Disclosure Statement

In compliance with the duty under 37 C.F.R. § 1.56, and in accordance with 37 C.F.R. §§ 1.97 et. seq., the enclosed Form SB08A and cited document are brought to the Office's attention for consideration in connection with the above-identified patent application. Applicant requests a copy of the From SB08A, initialed as considered by the Examiner, is returned with the next official communication. The cited document is submitted in compliance with 37 CFR § 1.97(b), after the mailing date of the first Office action on the merits, but prior to a final Office action. Accordingly, Applicant respectfully submits payment of $180.00.

CONCLUSIONS

Applicant respectfully asserts claims 1-14 and 21-32 are in condition for allowance. Should any issues or questions remain, the Examiner is encouraged to telephone the undersigned at (858) 623-9470 so they may be promptly resolved.

In the unlikely event the transmittal letter is separated from this document and the Office determines that an extension and/or other relief is required, Applicants petition for any required relief, including extensions of time, and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account 503473**.

Respectfully submitted,

Dated: June 26, 2006 By: /Bruce Grant/

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